ANTI HYPERTENSIVE EFFICACY OF CARDIOSELECTIVE 
BETA-BLOCKER ATENOLOL AND AMLODIPINE 
IN ESSENTIAL HYPERTENSIVE PATIENTS

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ABSTRACT
High blood pressure increases the risk of cardiovascular disease for millions of people worldwide and there is evidence that the problem is only getting worse. In the past decade, age adjusted rates of strokes incidence have risen. The incidence of end stage renal disease and the prevalence of heart failure have also increased. A major contributor to these trends is inadequate control of blood pressure in the population. The variety of treatments has been established with the passage of time from older to newer class. Researchers with passage of time proved on one side beneficiary drugs but also contraindicated in various types of patients. Keeping in view the necessity of treatment of hypertension at its initial stages in essential hypertensive patients to prevent cardiovascular complications in essential hypertensive patients. In present study the objective was to compare blood pressure lowering effects of cardio selective beta blocker Atenolol with calcium channel blocker Amlodipine in essential hypertensive patients.

Keywords:

INTRODUCTION
Hypertension affects almost 50 million people in the United States (U.S) and approximately 1 billion individuals' worldwide (Chobanian et al. 2003). There is much uncertainty about the path physiology of hypertension (Carretero and Oparil, 2000). Various population studies suggest that blood pressure is a continuous variable, with no absolute dividing line between normal and abnormal (Barriuso et al., 2003) The relation between cardiovascular risk and blood pressure is continuous; consistent across age groups, present in all ethnic groups, and independent of other risk factors (Staessen et al., 2005). Progress in understanding the pathogenesis of essential hypertension has been slow because essential hypertension is extremely complex at the molecular level (Brown 2006). The percentage of persons in whom hypertension is controlled is widely viewed as unsatisfactory and may in fact have decreased since 1990 Hyman et al., 2001). Current international hypertension guidelines (JNC–IV) recommended weight control, reduce intake of sodium chloride salt, reduce alcohol consumption and possibly increased dietary intake of potassium as nutritional approaches to prevent and treat hypertension Chobanian et al., 2003) the ultimate public health goal of anti-hypertensive therapy is the reduction of cardiovascular and renal morbidity and mortality (Chobanian et al. 2003). The benefits of drug intervention in hypertension is to reduce blood pressure are well established, especially in high-risk individuals (Dahlof et al., 2002). Beta-adrenoceptor blocking drugs have been shown safe and effective in the treatment of patients who have hypertension, angina pectoris, and glaucoma and migraine headaches (Frisman and Bronxy, 1998). Beta-blockers have long been considered to be well documented first-line drugs in the treatment of hypertension and it has been used as a reference drug in
randomized controlled trials of hypertension (Carlberg et al. 2004). The cardio selective beta-blocker has been shown safe and effective antihypertensive agents when administered either once daily or in divided doses (Turner et al. 1985). Among the different classes of drugs that are currently used in the treatment of hypertension calcium channel blockers (CCBs) play a special role because of their specific action on the constrictor tone of the vascular smooth muscle cells (Leonetti 2005). Among dihydropyridines, Amlodipine has been reported as an effective antihypertensive drug associated with regression of left ventricular hypertrophy and vascular hypertrophy, the anti-atherogenic and the remodeling effects (Schiffrin and Deng 1995).

SUBJECTS AND METHODS
This study was conducted in the department of pharmacology and therapeutics, Basic Medical Sciences Institute (BMSI), in collaboration with the department of medicine, Jinnah Post-graduate Medical Centre, Karachi, from June 2007 to January 2008. Eighty patients with newly diagnosed essential hypertension were initially enrolled in this study after taking informed and written consent, selected from medical OPD of JPMC. Out of these seventy-four patients were associated throughout the study period. Out of remaining six patients four has not come for follow-up in Amlodipine group two due to unknown reasons and two patients has complained of lethargy, dizziness, drowsiness and refused to continue the study while two patients were dropped in Atenolol group, due to gastric upset and headache. Following patients were included in the study: patients of either sex with newly diagnosed essential hypertension were initially enrolled in this study after taking informed and written consent, selected from medical OPD of JPMC. Out of these seventy-four patients were associated throughout the study period. Out of remaining six patients four has not come for follow-up in Amlodipine group two due to unknown reasons and two patients has complained of lethargy, dizziness, drowsiness and refused to continue the study while two patients were dropped in Atenolol group, due to gastric upset and headache. Following patients were included in the study: patients of either sex with newly diagnosed essential hypertension, patients aged between 20 – 70 years, patients having no history of using anti-hypertensive medications. The patients who were excluded from the study: patients having known history of allergy to beta-blockers or CCBs, patients having a history of hepatic or renal impairment, pregnant or lactating women, and patients who were already taking anti-hypertensive treatment. The safety and tolerability were assessed by spontaneous reports of adverse events as observed and reported by the patients and has been shown in table IC.

STUDY DESIGN
The study period was consisted of 12 weeks (90 days) with weekly follow-up visits of patients; but the observations of the parameters were recorded on day 0, day 45 and day 90 of the study period. The selected patients were divided into two groups. DR1 (Atenolol) and DR2 (Amlodipine). Forty patients with newly diagnosed essential hypertension with the above mentioned criteria were provided Tab. Atenolol 50 mg once a day for 90 days in DR 1 group; while forty patients with newly diagnosed essential hypertension were provided Tab. Amlodipine 10 mg once daily for 90 days in DR2 group. Following parameters were observed during study period, systolic blood pressure (SBP), diastolic blood pressure (DBP) and safety profile of the patients.

STATISTICAL ANALYSIS
All values have been expressed in standard error of mean (± SEM). The observations of the parameters were recorded in a tabulated form and paired students “t” test was used to analyze the data and observe the statistical significance of the results.

RESULTS
The results have been expressed as mean ± SEM (standard error of mean). Out of 40 patients on day 0, 38 patients were treated with DR1 till day 90. Out of 40 patients on DR2, 36 patients were treated till day 90. The mean systolic B.P. was decreased from 159.62 mmHg on day 0 to 145 mmHg on day 45 and 137.80 on day 90. This reduction was found statistically highly significant (p<0.001). The average Percentage reduction in systolic B.P was 14 from day 0 to day 90 as shown in Table 1A and Fig. 1A.
Out of 40 patients on DR2, 36 patients were treated till day 90\textsuperscript{th}. The mean systolic B.P. decreased from 160.12 ± 2.0 mmHg on day 0 to 147.0 ± 1.45 mmHg on day 45 and 140 ± 1.23 mmHg on day 90\textsuperscript{th} of the treatment. This reduction was found statistically highly significant (p<0.001). The average percentage reduction in systolic B.P was 12.56 % from day 0 to day 90\textsuperscript{th} of the treatment as shown in Table 1A and Fig. 1A.

Both Atenolol and Amlodipine decreased the mean diastolic B.P. In DR1 group, mean diastolic B.P. on day 0 was 97.75 mmHg which reduce to 92.10 mmHg on day 45 and 81.44 mmHg on day 90. This decrease in diastolic B.P was found statistically highly significant with a p-value (p<0.001) while in case of DR2 group mean diastolic B.P was decreased from 98.5 ± 0.61 mmHg on day 0 to 91.38 ± 0.67 mmHg on day 45 and 86.25 ±

### Table 1A
Changes in mean systolic B.P from Day 0 – Day 90, of the treatment with DR1, DR2 in essential hypertensive patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>At day 0 mmHg</th>
<th>At day 45 mmHg</th>
<th>At day 90 mmHg</th>
<th>Day 0-45</th>
<th>Day 45-90</th>
<th>Day 0-90</th>
<th>%change day 0 – day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR1</td>
<td>159.62±2.08 (40)</td>
<td>145±1.54 (38)</td>
<td>137.08±0.92 (38)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>↓14%</td>
</tr>
<tr>
<td>DR2</td>
<td>160.12±2.0 (40)</td>
<td>147.0±1.45 (36)</td>
<td>140±1.23 (36)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>↓12.56</td>
</tr>
</tbody>
</table>

Key:
- DR1 (Atenolol),
- DR 2 (Amlodipine)
- Values are in (mean ± SEM)
- All observations are in mmHg
- ↓ shows decrease in percentage

Fig. 1A. Changes in mean systolic B.P from day 0 – day 90 of treatment with DR1, DR2 in patients with essential Hypertension.
0.60 mmHg on day 90th of the treatment. This decrease was also observed statistically significant as depicted in Table 1B and Fig. 1B.

DISCUSSION

This study demonstrates significant changes in blood pressure with both Atenolol and Amlodipine in essential hypertension. Present study revealed that Atenolol and Amlodipine has significantly reduced the mean systolic and diastolic blood pressure in essential hypertensive patients. The results of both drug groups have shown statistically significant reduction with a P-value (P< 0.001). The results of our DR1 group are in accordance with the research clinical trials of Fogari et al. (2003), Devereux et al. (2003)

Table 1-B
Changes in mean diastolic B.P from day 0 – day 90 of the treatment with DR1 & DR2 in essential hypertensive patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>At day 0 mmHg</th>
<th>At day 45 mmHg</th>
<th>At day 90 mmHg</th>
<th>P – value</th>
<th>%change day 0 – day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0-45</td>
<td>Day 45-90</td>
<td>Day 0-90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DR1</td>
<td>97.37 ±0.80 (40)</td>
<td>92.77 ±0.75 (38)</td>
<td>81.44 ±0.73 (38)</td>
<td>&lt;0.001</td>
<td>&lt;0.001 &lt;0.001 ↓12%</td>
</tr>
<tr>
<td>DR2</td>
<td>98.5 ± 0.61 (40)</td>
<td>91.38 ± 0.67 (36)</td>
<td>86.25 ± 0.60 (36)</td>
<td>&lt;0.001</td>
<td>&lt;0.001 &lt;0.001 ↓%12.43</td>
</tr>
</tbody>
</table>

Key
- DR1 (Atenolol),
- DR2 (Amlodipine)
- Values are in (mean ± SEM)
- All observations are in mmHg
- ↓ shows decrease in p

Fig. 1-B. Changes in mean diastolic B.P from day 0 – day 90 of treatment with DR1, DR2 in patients with essential Hypertension.
Arif et al. (2006). The result of our DR2 group also matches with the studies conducted by Rashid et al (2004), Hoshide et al (2005) and Ishimitsu et al. (2005). The tolerability of the two drugs was not quite similar and the incidence of side effects reported by the patients during the whole duration of study was more observed and reported in DR2 group in comparison to DR 1 group.

**Table-1C**

| Observed and reported side effects with DR1 & DR2 in essential hypertensive patients |
|---------------------------------|-----------|-----------|
| Drowsiness                      | 0         | 01        |
| Constipation                    | 0         | 02        |
| Headache                        | 01        | 01        |
| Dizziness                       | 0         | 02        |
| Abdominal pain                  | 01        | 0         |
| Backache                        | 01        | 0         |
| Edema                           | 0         | 0         |
| Nausea / Vomiting               | 0         | 01        |
| Total Patients                  | 04        | 07        |

**CONCLUSION**

As far as the antihypertensive efficacy is concerned, there were no clinically relevant differences between Atenolol and Amlodipine. However, Atenolol is cost-effective for the treatment of essential hypertension in comparison to conventional anti-hypertensive treatment.

**REFERENCES**


